# UNITED STATES PATENT AND TRADEMARK OFFICE

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/001,934 | 11/15/2001 | Zoltan Nagy | GPCG-P01-003 | 8886 |

| 28120 | 7590 | 09/25/2006 |
|---|---|---|

FISH & NEAVE IP GROUP
ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA  02110-2624

| EXAMINER |
|---|
| CANELLA, KAREN A |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1643 | |

DATE MAILED: 09/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
  Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☐ Responsive to communication(s) filed on _____.
2a) ☐ This action is **FINAL.**  2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) ☐ Claim(s) *See Continuation Sheet* is/are pending in the application.
    4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☐ Claim(s) *11,18,20,22-24,26,28,33-36,55,56,61,67,71,73,121 and 123* is/are rejected.
7) ☐ Claim(s) *See Continuation Sheet* is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☒ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
    a) ☐ All   b) ☐ Some * c) ☐ None of:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____.
      3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
    * See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
    Paper No(s)/Mail Date *1/28/04 7/3/06*.
4) ☐ Interview Summary (PTO-413)
    Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Disposition of Claims: Claims pending in the application are 7-29,33-37,43,55,56,59-63,67,71-79,81-87,92-95,117,118 and 120-129.

Continuation of Disposition of Claims: Claims objected to are 7-10,12-17,19,21,25,27,29,37,43,59,60,62,63,72,74-77,79,81-87,92-95,117,118,120,122 and 124-129.

Continuation of Attachment(s) 6). Other:  Raw Sequence Listing Error Report.

## DETAILED ACTION

Claims 22, 23, 67 and 81 have been amended. Claims 7-29, 33-37, 43, 55, 56, 59-63, 67, 71-79, 81-87, 92-95, 117, 118 and 120-129 are pending and under consideration.

Text of Title 35, U.S. code not found in this action can be found in a prior action.

The specification is objected to for lack of compliance to the Sequence Rules. The CRF for the Sequence Listing submitted January 28, 2004 has not been entered due to the errors outlines on the attached Raw Sequence Error Report.

Appropriate correction is required.

Claims 7-29, 33-37, 43, 55, 56, 59-63, 67, 71-79, 81-87, 92-95, 117, 118, 120-129 are objected to because of the following informalities: The claims do not comply with the Sequence rules for the reasons set forth above.. Appropriate correction is required.

Claims 11, 18, 22-24, 26, 28, 33-36, 55, 56, 67, 71, 73, 121 and 123 are rejected under 35 U.S.C. 102(b) as being anticipated by Viken et al (Human Immunology, 1995, Vol. 43, pp. 200-206, reference of the IDS filed February 6, 2003).

Viken et al disclose the human IgM antibody, 5643, wherein said antibody is cytotoxic against the B-lymphoblastoid cell lines of BTB, BM9 and Madura (page 200, second column and page 201, Table 1) which fulfills the limitations of claims 73. Viken et al disclose that said antibody is specific to HLA-DR8 0801 (page 202, under the heading "Specificity of mAb 5643"). Viken et al disclose the use of the 5643 hybridoma supernatant in HLA typing of class II positive cells which fulfills the specific embodiment of claim 55 requiring a diagnostic composition. Viken et al disclose that the 5643 antibody does not bind the 0802 or 0804 subtypes of DR8 and that the only difference between these two subtypes is a ser to Asp substitution at residue 57 and a Phe to Ile substitution at residue 67 on the beta chain (page 202, under the heading "Specificity of mAb 5643"). Viken et al also disclose that another mAb, L243, which binds to the DR alpha chain inhibits binding of the 5643 antibody (page 205, second full paragraph). The 5643 antibody fulfills the specific embodiment of claim 33 because

a whole IgM antibody is a multivalent polypeptide including at least the F(ab')2 portion of the antibody. The 5643 antibody fulfills the specific embodiments of claims 34, 35 and 56 because an IgM antibody includes disulphide bonds and the "J" chain, both of which can be construed as a cross-linking moiety (Roitt et al, Immunology (text), 1993, page 4.5, figure 4.9) which was confirmed prior to binding to the target cell.

Viken et al do not specifically disclose the epitope of the 5643 antibody, however, it would be reasonable to conclude that the epitope was not a linear epitope and comprised amino acid residues on both the alpha and the beta chains because binding of the 5643 antibody was influenced by amino acid substitutions to the beta chain, as well as competition from a known antibody which bound to the alpha chain. Viken et al do not specifically disclose the sequence of the antigen binding domains of the 5643 antibody, however, the claimed antibodies appear to be the same as the prior art antibodies in terms of human origin, target antigen and cytotoxicity to lymphoid cells, absent a showing of unobvious differences. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claims 11, 20, 22-24, 26, 28, 33-36, 55, 56, 61, 67, 73 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Kolstad et al (Tissue Antigens, 1988, Vol. 31, pp. 90-97).

Kolstad et al disclose the cytotoxic human IgM antibody, TrH6, which binds specifically kills B cells expressing HLA-DR52W (page 91, under the heading of "Microcytotoxicity assays" and page 92, Table 1) which fulfills the limitation of claim 20 and claim 78. Kolstad et al disclose that the TrH6 antibody was iodine labeled (page 91 under the heading of "Purification and iodination of mAbs") which fulfills the specific embodiment of claim 61 requiring the detectable label. The TrH6 antibody fulfills the specific embodiments of claims 34, 35 and 56 because an IgM antibody includes disulphide bonds and the "J" chain, both of which can be

construed as a cross-linking moiety (Roitt et al, Immunology (text), 1993, page 4.5, figure 4.9) which was confirmed prior to binding to the target cell.

Kolstad et al do not specifically disclose the sequence of the antigen binding domains of the TrH6 antibody, or the however, the claimed antibodies appears to be the same as the prior art antibodies in terms of human origin, target antigen and cytotoxicity to lymphoid cells, absent a showing of unobvious differences. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

All other rejections and objections as set forth in the previous Office action are withdrawn in light of applicants arguments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.
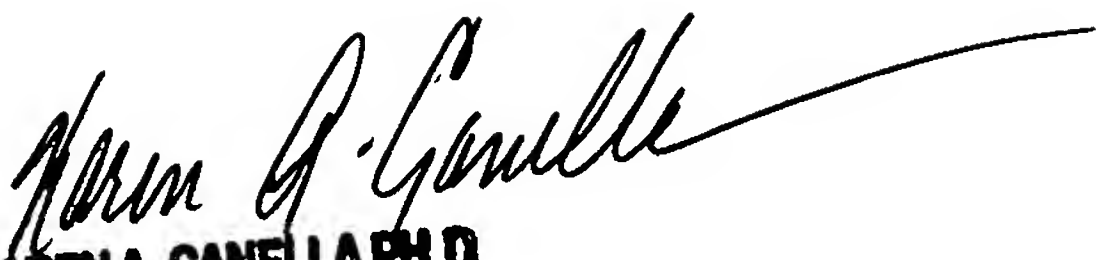
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen A. Canella, Ph.D.

9/17/2006

KAREN A. CANELLA PH.D
PRIMARY EXAMINER
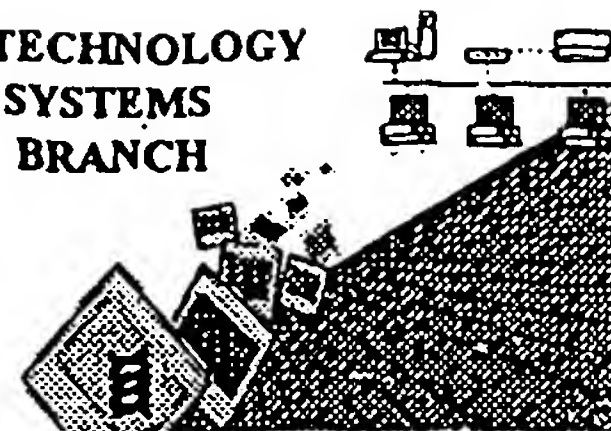
# RAW SEQUENCE LISTING
# ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: _10/001,9346_
Source: _1FW16_
Date Processed by STIC: _2/3/04_

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:
1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 703-308-4212; FAX: 703-308-4221
*Effective 12/13/03*: TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE <u>CHECKER VERSION 4.1 PROGRAM</u>, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:
        **http://www.uspto.gov/web/offices/pac/checker/chkr41note.htm**

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail. Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom. Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (**<http://www.uspto.gov/ebc/efs/downloads/documents.htm>** , EFS Submission User Manual - cPAVE)
2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. Hand Carry directly to (EFFECTIVE 12/01/03):
   U.S. Patent and Trademark Office, Box Sequence, Customer Window, Lobby, Room 1B03, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202
4. Federal Express, United Parcel Service, or other delivery service to: U.S. Patent and Trademark Office, Box Sequence, Room 4B03-Mailroom, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202

Revised 10/08/03
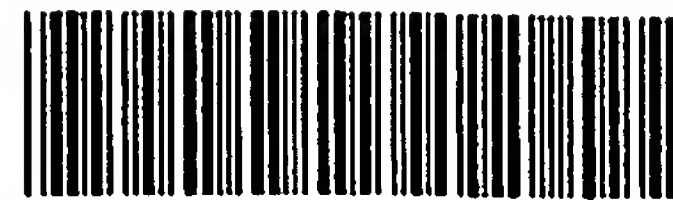
**IFW16**

RAW SEQUENCE LISTING       DATE: 02/03/2004
PATENT APPLICATION:   **US/10/001,934B**      TIME: 11:42:46

Input Set : **N:\DA\pto.da.txt**
Output Set: **N:\CRF4\01292004\J001934B.raw**

```
   4 <110> APPLICANT: NAGY et al.
   6 <120> TITLE OF INVENTION: HUMAN POLYPEPTIDES CAUSING OR LEADING TO THE KILLING
   7        OF CELLS INCLUDING LYMPHOID TUMOR CELLS
   9 <130> FILE REFERENCE: GPCG-P01-003
  11 <140> CURRENT APPLICATION NUMBER: 10/001934B
  12 <141> CURRENT FILING DATE: 2001-11-15
  14 <150> PRIOR APPLICATION NUMBER: PCT/US01/15625
  15 <151> PRIOR FILING DATE: 2001-05-14
  17 <150> PRIOR APPLICATION NUMBER: EP 00 11 0065.0
  18 <151> PRIOR FILING DATE: 2000-05-12
  20 <150> PRIOR APPLICATION NUMBER: US 60/238,762
  21 <151> PRIOR FILING DATE: 2000-10-06
  23 <160> NUMBER OF SEQ ID NOS: 62
  25 <170> SOFTWARE: PatentIn version 3.2
  28 <210> SEQ ID NO: 1
  29 <211> LENGTH: 10
  30 <212> TYPE: PRT
  31 <213> ORGANISM: artificial sequence
  33 <220> FEATURE:
W--> 34 <221> NAME/KEY: VHconCDR3
  35 <222> LOCATION: (1)..(10)
  36 <223> OTHER INFORMATION: "Xaa" represents any amino acid residue
  38 <400> SEQUENCE: 1
W--> 40 Xaa Xaa Xaa Xaa Arg Gly Xaa Phe Asp Xaa
  41 1               5                   10
  44 <210> SEQ ID NO: 2
  45 <211> LENGTH: 8
  46 <212> TYPE: PRT
  47 <213> ORGANISM: artificial sequence
  49 <220> FEATURE:
W--> 50 <221> NAME/KEY: VLconCDR3
  51 <222> LOCATION: (1)..(8)
  52 <223> OTHER INFORMATION: "Xaa" represents any amino acid residue
  55 <400> SEQUENCE: 2
W--> 57 Gln Ser Tyr Asp Xaa Xaa Xaa Xaa
  58 1               5
  61 <210> SEQ ID NO: 3
  62 <211> LENGTH: 10
  63 <212> TYPE: PRT
  64 <213> ORGANISM: artificial sequence
  66 <220> FEATURE:
W--> 67 <221> NAME/KEY: MS-GPC8-VH-CDR3,MS-GPC8-1-VH-CDR3,MS-GPC8-6-VH-CDR3, MS-GPC8-9-VH-
W--> 68       CDR3,MS-GPC8-10-VH-CDR3,MS-GPC8-17-VH-CDR3, MS-GPC8-18-VH-CDR3, MS-GPC8-27-VH-
```

*[Handwritten annotations:]*
Suggestion: Consult Sequence Rules.
see pp 1-6
Please Explain
Does Not Comply
Corrected Diskette Needed
source of genetic material on <223>
This is not a valid <221> response. See Sequence Rules.
line (per Sequence Rules) see p.6 for error explanation (global error)
same error
Same error as Sequence 1.
same error
same

RAW SEQUENCE LISTING                    DATE: 02/03/2004
PATENT APPLICATION:  US/10/001,934B     TIME: 11:42:46

Input Set : N:\DA\pto.da.txt
Output Set: N:\CRF4\01292004\J001934B.raw          *same*

```
W--> 69      CDR3, MS-GPC8-6-2-VH-CDR3, MS-GPC8-6-13-VH-CDR3, MS-GPC8-6-19-VH-CDR3, MS-GPC8-
W--> 70      6-27-VH-CDR3, MS-GPC8-6-45-VH-CDR3, MS-GPC8-10-57-VH-CDR3, MS-GPC8-27-7-VH-CDR3,
W--> 71      MS-GPC8-27-10-VH-CDR3, MS-GPC8-27-41-VH-CDR3, MS-GPC8-6-47-VH-CDR3
     72 <222> LOCATION: (1)..(10)
W--> 74 <223> OTHER INFORMATION:
W--> 74 <400> 3
     76 Ser Pro Arg Tyr Arg Gly Ala Phe Asp Tyr
     77 1               5                   10
     80 <210> SEQ ID NO: 4
     81 <211> LENGTH: 8
     82 <212> TYPE: PRT                              same
     83 <213> ORGANISM: artificial sequence
     85 <220> FEATURE:
W--> 86 <221> NAME/KEY: MS-GPC8-10-VL-CDR3,MS-GPC8-10-57-VL-CDR3    same
     87 <222> LOCATION: (1)..(8)
W--> 89 <223> OTHER INFORMATION:
W--> 89 <400> 4
     90 Gln Ser Tyr Asp Leu Ile Arg His
     91 1               5
     94 <210> SEQ ID NO: 5
     95 <211> LENGTH: 8
     96 <212> TYPE: PRT                              same
     97 <213> ORGANISM: artificial sequence
     99 <220> FEATURE:                                        same
W--> 100 <221> NAME/KEY: MS-GPC8-27-VL-CDR3,MS-GPC8-27-7-VL-CDR3,MS-GPC8-27-10-VL-CDR3,MS-
GPC8-27-
W--> 101       41-VL-CDR3
     102 <222> LOCATION: (1)..(8)
W--> 104 <223> OTHER INFORMATION:
W--> 104 <400> 5
     105 Gln Ser Tyr Asp Met Asn Val His
     106 1               5
     109 <210> SEQ ID NO: 6
     110 <211> LENGTH: 13
     111 <212> TYPE: PRT                             same
     112 <213> ORGANISM: artificial sequence
     114 <220> FEATURE:
W--> 115 <221> NAME/KEY: VLconCDR1
     116 <222> LOCATION: (1)..(13)
     118 <220> FEATURE:
W--> 119 <221> NAME/KEY:
     120 <222> LOCATION: (4)..(5)
     121 <223> OTHER INFORMATION: "Xaa" represents any amino acid residue
     123 <220> FEATURE:
W--> 124 <221> NAME/KEY:
     125 <222> LOCATION: (9)..(9)
     126 <223> OTHER INFORMATION: "Xaa" represents any amino acid residue
     128 <220> FEATURE:
W--> 129 <221> NAME/KEY:
     130 <222> LOCATION: (13)..(13)
```

RAW SEQUENCE LISTING         DATE: 02/03/2004
PATENT APPLICATION:  US/10/001,934B     TIME: 11:42:46

Input Set : **N:\DA\pto.da.txt**
Output Set: **N:\CRF4\01292004\J001934B.raw**

```
      131 <223> OTHER INFORMATION: "Xaa" represents any amino acid residue
      133 <400> SEQUENCE: 6
W-->  134 Ser Gly Ser Xaa Xaa Asn Ile Gly Xaa Asn Tyr Val Xaa
      135 1              5                  10
      138 <210> SEQ ID NO: 7
      139 <211> LENGTH: 13                           same
      140 <212> TYPE: PRT
      141 <213> ORGANISM: artificial sequence
      143 <220> FEATURE:
W-->  144 <221> NAME/KEY: MS-GPC-8-10-57-VL-CDR1, MS-GPC-8-27-41-VL-CDR1    same
      145 <222> LOCATION: (1)..(13)
W-->  147 <223> OTHER INFORMATION:
W-->  147 <400> 7
      148 Ser Gly Ser Glu Ser Asn Ile Gly Asn Asn Tyr Val Gln
      149 1              5                  10
      152 <210> SEQ ID NO: 8
      153 <211> LENGTH: 8                            same
      154 <212> TYPE: PRT
      155 <213> ORGANISM: artificial sequence
      157 <220> FEATURE:
W-->  158 <221> NAME/KEY: Streptaq    same
      159 <222> LOCATION: (1)..(8)
W-->  161 <223> OTHER INFORMATION:
W-->  161 <400> 8
      163 Trp Ser His Pro Gln Phe Glu Lys
      164 1              5
      166 <210> SEQ ID NO: 9
      167 <211> LENGTH: 4                            same
      168 <212> TYPE: PRT
      169 <213> ORGANISM: artificial sequence
      171 <220> FEATURE:
W-->  172 <221> NAME/KEY: FLAG   same
      173 <222> LOCATION: (1)..(4)
W-->  175 <223> OTHER INFORMATION:
W-->  175 <400> 9
      177 Asp Tyr Lys Asp
      178 1
      181 <210> SEQ ID NO: 10
      182 <211> LENGTH: 17                           same
      183 <212> TYPE: DNA
      184 <213> ORGANISM: artificial sequence
      186 <220> FEATURE:
W-->  187 <221> NAME/KEY: PrimerCRT5   same
      188 <222> LOCATION: (1)..(17)
W-->  190 <223> OTHER INFORMATION:
W-->  190 <400> 10
      191 gtggtggttc cgatatc                                        17
      194 <210> SEQ ID NO: 11
      195 <211> LENGTH: 44
```

RAW SEQUENCE LISTING                 DATE: 02/03/2004
PATENT APPLICATION:  US/10/001,934B        TIME: 11:42:46

Input Set : N:\DA\pto.da.txt
Output Set: N:\CRF4\01292004\J001934B.raw

```
        196 <212> TYPE: DNA
        197 <213> ORGANISM: artificial sequence          same
        199 <220> FEATURE:
W--> 200 <221> NAME/KEY: PrimerCRT6          same
        201 <222> LOCATION: (1)..(44)
W--> 203 <223> OTHER INFORMATION:
W--> 203 <400> 11
        204 agcgtcacac tcggtgcggc tttcggctgg ccaagaacgg gtta          44
        207 <210> SEQ ID NO: 12
        208 <211> LENGTH: 13
        209 <212> TYPE: PRT
        210 <213> ORGANISM: artificial sequence     same     same
        212 <220> FEATURE:
W--> 213 <221> NAME/KEY: MS-GPC1-VL-CDR1,MS-GPC8-VL-CDR1,MS-GPC10-VL-CDR1,MS-GPC8-1-VL-
CDR1,MS-
W--> 214     GPC8-6-VL-CDR1,MS-GPC8-9-VL-CDR1,MS-GPC8-10-VL-CDR1, MS-GPC8-17-VL-CDR1,MS-
GPC8-
W--> 215     18-VL-CDR1,MS-GPC8-27-VL-CDR1,
        216 <222> LOCATION: (1)..(13)
W--> 218 <223> OTHER INFORMATION:
W--> 218 <400> 12
        219 Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Tyr Val Ser
        220 1              5              10
        223 <210> SEQ ID NO: 13
        224 <211> LENGTH: 13
        225 <212> TYPE: PRT
        226 <213> ORGANISM: artificial sequence     same
        228 <220> FEATURE:
W--> 229 <221> NAME/KEY: MS-GPC8-6-2-VL-CDR1
        230 <222> LOCATION: (1)..(13)
W--> 232 <223> OTHER INFORMATION:
W--> 232 <400> 13
        233 Ser Gly Ser Glu Ser Asn Ile Gly Ser Asn Tyr Val His
        234 1              5              10
        237 <210> SEQ ID NO: 14
        238 <211> LENGTH: 13
        239 <212> TYPE: PRT
        240 <213> ORGANISM: artificial sequence
        242 <220> FEATURE:
W--> 243 <221> NAME/KEY: MS-GPC8-6-19-VL-CDR1          same
        244 <222> LOCATION: (1)..(13)
W--> 246 <223> OTHER INFORMATION:
W--> 246 <400> 14
        247 Ser Gly Ser Glu Ser Asn Ile Gly Ser Asn Tyr Val Ala
        248 1              5              10
        251 <210> SEQ ID NO: 15
        252 <211> LENGTH: 13
        253 <212> TYPE: PRT
        254 <213> ORGANISM: artificial sequence      same
        256 <220> FEATURE:
W--> 257 <221> NAME/KEY: MS-GPC8-6-27-VL-CDR1
```

RAW SEQUENCE LISTING                    DATE: 02/03/2004
PATENT APPLICATION:  US/10/001,934B      TIME: 11:42:46

Input Set : **N:\DA\pto.da.txt**
Output Set: **N:\CRF4\01292004\J001934B.raw**

```
        258 <222> LOCATION: (1)..(13)
W--> 260 <223> OTHER INFORMATION:
W--> 260 <400> 15
        261 Ser Gly Ser Asp Ser Asn Ile Gly Ala Asn Tyr Val Thr
        262 1           5               10
        265 <210> SEQ ID NO: 16
        266 <211> LENGTH: 13
        267 <212> TYPE: PRT
        268 <213> ORGANISM: artificial sequence        same
        270 <220> FEATURE:
W--> 271 <221> NAME/KEY: MS-GPC8-6-45-VL-CDR1
        272 <222> LOCATION: (1)..(13)
W--> 274 <223> OTHER INFORMATION:
W--> 274 <400> 16
        275 Ser Gly Ser Glu Pro Asn Ile Gly Ser Asn Tyr Val Phe
        276 1           5               10
        279 <210> SEQ ID NO: 17
        280 <211> LENGTH: 13
        281 <212> TYPE: PRT
        282 <213> ORGANISM artificial sequence          same
        284 <220> FEATURE:
W--> 285 <221> NAME/KEY: MS-GPC8-27-7-VL-CDR1
        286 <222> LOCATION: (1)..(13)
W--> 288 <223> OTHER INFORMATION:
W--> 288 <400> 17
        289 Ser Gly Ser Glu Ser Asn Ile Gly Asn Asn Tyr Val Gly
        290 1           5               10
        293 <210> SEQ ID NO: 18
        294 <211> LENGTH: 13
        295 <212> TYPE: PRT
        296 <213> ORGANISM: artificial sequence         same
        298 <220> FEATURE:
W--> 299 <221> NAME/KEY: MS-GPC8-27-10-VL-CDR1
        300 <222> LOCATION: (1)..(13)
W--> 302 <223> OTHER INFORMATION:
W--> 302 <400> 18
        303 Ser Gly Ser Glu Ser Asn Ile Gly Ala Asn Tyr Val Asn
        304 1           5               10
        307 <210> SEQ ID NO: 19
        308 <211> LENGTH: 10
        309 <212> TYPE: PRT
        310 <213> ORGANISM artificial sequence
        312 <220> FEATURE:
W--> 313 <221> NAME/KEY: MS-GPC1-VH-CDR3                 same
        314 <222> LOCATION: (1)..(10)
W--> 316 <223> OTHER INFORMATION:
W--> 316 <400> 19
        318 Gln Tyr Gly His Arg Gly Gly Phe Asp His
        319 1           5               10
```

RAW SEQUENCE LISTING ERROR SUMMARY     DATE: 02/03/2004
PATENT APPLICATION: US/10/001,934B     TIME: 11:42:47

Input Set : N:\DA\pto.da.txt
Output Set: N:\CRF4\01292004\J001934B.raw

**Please Note:**
Use of n and/or Xaa have been detected in the Sequence Listing. Please review the
Sequence Listing to ensure that a corresponding explanation is presented in the <220>
to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:1; Xaa Pos. 1,2,3,4,7,10
Seq#:2; Xaa Pos. 5,6,7,8
Seq#:6; Xaa Pos. 4,5,9,13

**Invalid Line Length:**
The rules require that a line not exceed 72 characters in length. This includes spaces.

Seq#:3; Line(s) 70
Seq#:5; Line(s) 100
Seq#:12; Line(s) 214
Seq#:41; Line(s) 1333,1334
Seq#:60; Line(s) 1938

**Use of <220> Feature(NEW RULES):** *error explanation*
Sequence(s)__are missing the <220> Feature and associated headings.
Use of <220> to <223> is MANDATORY if <213> ORGANISM is "Artificial Sequence"
or"Unknown". Please explain source of genetic material in <220> to <223>
section (See "Federal Register," 6/01/98, Vol. 63, No. 104,pp.29631-32)
(Sec.1.823 of new Rules)

Seq#:3,4,5,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29
Seq#:30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53
Seq#:54,55,56,57,58,59,60,61,62 ,1,2,6

**VERIFICATION SUMMARY**  DATE: 02/03/2004
PATENT APPLICATION:  **US/10/001,934B**   TIME: 11:42:47

Input Set : **N:\DA\pto.da.txt**
Output Set: **N:\CRF4\01292004\J001934B.raw**

L:34 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:1
L:40 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:0
L:50 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:2
L:57 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:0
L:67 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:3
L:68 M:257 W: Feature value mis-spelled or invalid, Describe feature in <223> for SEQ ID#:3
L:69 M:257 W: Feature value mis-spelled or invalid, Describe feature in <223> for SEQ ID#:3
L:70 M:257 W: Feature value mis-spelled or invalid, Describe feature in <223> for SEQ ID#:3
L:71 M:257 W: Feature value mis-spelled or invalid, Describe feature in <223> for SEQ ID#:3
L:74 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:3, <213>
ORGANISM:artificial sequence
L:74 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:3,Line#:74
L:86 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:4
L:89 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:4, <213>
ORGANISM:artificial sequence
L:89 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:4,Line#:89
L:100 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:5
L:101 M:257 W: Feature value mis-spelled or invalid, Describe feature in <223> for SEQ ID#:5
L:104 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:5, <213>
ORGANISM:artificial sequence
L:104 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:5,Line#:104
L:115 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:6
L:119 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:6
L:124 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:6
L:129 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:6
L:134 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:6 after pos.:0
L:144 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:7
L:147 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:7, <213>
ORGANISM:artificial sequence
L:147 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:7,Line#:147
L:158 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:8
L:161 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:8, <213>
ORGANISM:artificial sequence
L:161 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:8,Line#:161
L:172 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:9
L:175 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:9, <213>
ORGANISM:artificial sequence
L:175 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:9,Line#:175
L:187 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:10
L:190 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:10, <213>
ORGANISM:artificial sequence
L:190 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:10,Line#:190
L:200 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:11
L:203 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:11, <213>
ORGANISM:artificial sequence
L:203 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:11,Line#:203
L:213 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:12
L:214 M:257 W: Feature value mis-spelled or invalid, Describe feature in <223> for SEQ ID#:12
L:215 M:257 W: Feature value mis-spelled or invalid, Describe feature in <223> for SEQ ID#:12
L:218 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:12, <213>
ORGANISM:artificial sequence
L:218 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:12,Line#:218
L:229 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:13

L:232 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:13, <213>
ORGANISM:artificial sequence
L:232 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:13,Line#:232
L:243 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:14
L:246 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:14, <213>
ORGANISM:artificial sequence

**VERIFICATION SUMMARY**          DATE: 02/03/2004
PATENT APPLICATION:  **US/10/001,934B**      TIME: 11:42:47

Input Set : **N:\DA\pto.da.txt**
Output Set: **N:\CRF4\01292004\J001934B.raw**

```
L:246 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:14,Line#:246
L:257 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:15
L:260 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:15, <213>
ORGANISM:artificial sequence
L:260 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:15,Line#:260
L:271 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:16
L:274 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:16, <213>
ORGANISM:artificial sequence
L:274 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:16,Line#:274
L:285 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:17
L:288 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:17, <213>
ORGANISM:artificial sequence
L:288 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:17,Line#:288
L:299 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:18
L:302 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:18, <213>
ORGANISM:artificial sequence
L:302 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:18,Line#:302
L:313 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:19
L:316 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:19, <213>
ORGANISM:artificial sequence
L:316 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:19,Line#:316
L:328 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:20
L:331 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:20, <213>
ORGANISM:artificial sequence
L:331 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:20,Line#:331
L:343 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:21
L:346 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:21, <213>
ORGANISM:artificial sequence
L:346 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:21,Line#:346
L:358 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:22
L:361 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:22, <213>
ORGANISM:artificial sequence
L:361 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:22,Line#:361
L:373 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:23
L:376 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:23, <213>
ORGANISM:artificial sequence
L:376 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:23,Line#:376
L:388 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:24
L:391 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:24, <213>
ORGANISM:artificial sequence
L:391 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:24,Line#:391
L:403 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:25
L:406 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:25, <213>
ORGANISM:artificial sequence
L:406 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:25,Line#:406
L:417 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:26
L:420 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:26, <213>
ORGANISM:artificial sequence
L:420 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:26,Line#:420
L:432 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:27
L:435 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:27, <213>
ORGANISM:artificial sequence
L:435 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:27,Line#:435
```

```
L:446 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:28
L:449 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:28, <213>
ORGANISM:artificial sequence
L:449 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:28,Line#:449
L:479 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:29
L:494 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:30
L:508 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:31
L:540 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:32
L:573 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:33
L:704 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:34
```

**VERIFICATION SUMMARY**                    DATE: 02/03/2004
PATENT APPLICATION:  **US/10/001,934B**        TIME: 11:42:47

Input Set : **N:\DA\pto.da.txt**
Output Set: **N:\CRF4\01292004\J001934B.raw**

L:864 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:35
L:1043 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:36
L:1194 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:37
L:1230 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:38
L:1263 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:39
L:1299 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:40